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Executive Report

California Department of Public Health – Department of Health Care Services Antipsychotic Collaborative

Center for Health Care Quality

The California Department of Public Health Center for Health Care Quality (CHCQ) is responsible for regulatory oversight of health facilities, health professionals, and clinical and public health laboratories to secure safe, effective, and quality health care for all Californians.

Through its Licensing and Certification program and Laboratory Field Services Program, the Center for Health Care Quality plays a critical role in the protection of patient safety by evaluating applicant health facilities, agencies, clinical laboratories, and professionals for compliance with state laws and regulations in order to license, certify, or register them. CHCQ also investigates complaints, certifies health facilities' and agencies' compliance with federal laws and regulations, and oversees the education, training, and criminal record clearance of nursing home administrators, certified nurse assistants, home health aides, hemodialysis technicians, clinical laboratory scientists, and phlebotomists.

Quality of care concerns regarding the use of antipsychotic drug use in nursing homes have led to the development of a California Department of Public Health/California Department of Health Care Services collaborative to review the use of antipsychotic medications in California nursing homes and recommend solutions.

This executive report presents an analysis of the findings of the California Department of Public Health (CDPH) and California Department of Health Care Services (DHCS) antipsychotic collaborative (herein forth referred to as the collaborative). The findings of the collaborative are accompanied by recommendations to address identified quality of care issues, with the intent to reduce inappropriate antipsychotic medication use in California nursing homes, thereby reducing the risk of unnecessary side effects and excess health care costs associated with the misuse of these medications.

CDPH Pharmaceutical Consultants (PCs) have identified multiple quality of care issues related to antipsychotic use during 42 nursing home antipsychotic collaborative

investigations over a 16-month period. These investigative findings demonstrate an opportunity for improvement in the use of these medications as related to:

- Providing residents and their designated representatives with accurate and complete information to make informed decisions regarding the use of these medications;
- Ensuring appropriate use of antipsychotic medications by considering non-pharmacologic interventions, as well as the risks and benefits associated with the medication prior to using the antipsychotic;
- Developing and implementing complete and accurate antipsychotic care plans; and,
- Provision of quality consultant pharmacist services.

This executive report is a response to an Administration directive in 2009, calling for a study of potential inappropriate use of psychotherapeutic medications.

Background

Antipsychotic Medication Use in Nursing Homes

Nationwide, nursing home residents (also referred to as “patients” in this report) continue to be prescribed antipsychotic medications at a high rate, with more than one of every four Medicare beneficiaries (27.6%) receiving these medications, and of these, more than half (58.2%) represent inappropriate use (e.g., excessive dose, without adequate documentation of the indication for use), thereby exposing them to unnecessary side effects and potential harm.^[1]

According to CMS’s Online Survey, Certification and Reporting (OSCAR) data, the use of antipsychotic medications in California nursing homes has remained relatively unchanged over the last three years with an average of 24.2% nursing home residents—approximately one in four—receiving these drugs.^[2] This utilization rate represents all uses of antipsychotic medications, both appropriate and potentially inappropriate, in all nursing home residents.

Inappropriate prescribing of antipsychotic medications in nursing homes has long been considered a marker of suboptimal care.^[3, 4] In April 2005, the Food and Drug Administration (FDA) notified healthcare professionals that patients with dementia-related psychosis treated with atypical (second-generation) antipsychotic drugs are at an increased risk of death.^[5] In June 2008, the FDA again notified healthcare professionals that both conventional (first-generation) and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis.^[6] (See Appendix A, “What are antipsychotic medications?”)

In spite of the FDA's strong warnings, use of antipsychotic medications in nursing homes continues to remain considerable, as evidenced by the recent audit by the US Department of Health and Human Services Office of Inspector General (HHS-OIG), mainly because of the continued growth in the number of elderly persons with dementia, the perceived need for some type of chemical intervention in patients with severe persistent behavioral symptoms, and a lack of effective therapeutic and/or behavioral interventions.^[7] The report identified a number of key findings including: 83% of Medicare beneficiaries receiving atypical antipsychotic medications were for non-FDA ("off-label") approved indications (e.g., dementia-related behaviors), and 22% were not administered in accordance with federal regulations for nursing homes as set forth by the Centers for Medicare and Medicaid Services (CMS).

Inappropriate antipsychotic medication use, as defined by CMS,^[8] includes one or more of the following:

- Without an adequate indication for use;
- Use for an excessive duration without gradual dose reduction attempts;
- Duplicate drug therapy (use of two or more antipsychotics without clinical justification substantiating the need for polypharmacy);
- Without adequate monitoring for therapeutic efficacy and/or adverse consequences;
- In excessive dose based on the clinical indication and/or the condition of the resident; and,
- In the presence of adverse consequences that indicate the antipsychotic dose should be reduced or discontinued.

Antipsychotic polytherapy or polypharmacy refers to the use of two or more antipsychotics concurrently in a single patient. Treatment guidelines support monotherapy with antipsychotic medications;^[9] a clear role for the use of polytherapy has not been defined. Several reports demonstrate the prescribing of multiple antipsychotic medications is an increasing trend, occurring in up to 40% of inpatients and 11%-35% of outpatients receiving these medications.^[10, 11, 12] In the majority of clinical circumstances, the use of antipsychotic polytherapy increases the risk of side effects without providing additional benefit.^[13] The reduction in use of polytherapy holds promise for reducing the direct cost of therapy of these expensive medications, while also potentially reducing direct and indirect costs attributed to drug interactions and untoward side effects consequent to additive pharmacologic effects.^[14]

CDPH/DHCS Antipsychotic Collaborative

Secondary to ongoing concerns related to inappropriate antipsychotic medication use in California's nursing home residents, CDPH's Licensing and Certification (L&C) Pharmaceutical Consultant (PC) Unit, along with DHCS Pharmacy Policy and Benefits Division (PBD) and California Mental Health Care Management Program (CalMEND) personnel, developed the collaborative framework to encourage appropriate antipsychotic medication use in California's nursing homes. To achieve this goal, the collaborative combines each department's unique resources to identify and address inappropriate use of antipsychotic medications.

L&C pharmaceutical consultants, utilizing DHCS Medi-Cal prescription claims data, conduct onsite nursing home clinical record reviews to determine the appropriateness of antipsychotic use. When regulatory non-compliances are identified, CDPH issues a "Statement of Deficiencies." The facility is required to submit a "Plan of Correction," which is an outline of how the facility expects to correct the identified regulatory non-compliance and prevent a reoccurrence. These enforcement actions are intended to improve patient care and reduce health care associated costs at the individual facility level.

Beginning in May 2010, the collaborative conducted 42 on-site surveys in nursing homes based on DHCS claims data. The investigations focused on residents who were receiving two or more antipsychotics concurrently (polypharmacy), aged 55 years or greater, with a diagnosis of serious mental illness (SMI) and/or dementia; and patients who are 65 years of age or greater, receiving only one antipsychotic with a diagnosis of dementia (no SMI). According to DHCS's guidelines, serious mental illnesses include major depression, schizophrenia, bipolar disorder, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, and borderline personality disorder.

The PC surveyor assesses for compliance with pertinent regulations and statutes that are related to the provision of nursing, medical, and pharmaceutical care and services, as well as those associated with informed consent.

Inappropriate Antipsychotic Use Findings

Of the 42 investigations, 29 (69%) resulted in deficiencies related to inappropriate antipsychotic use, impacting 52 nursing home residents. Review of these 29 investigations in which inappropriate antipsychotic use was identified revealed the following:

- In 23 of 27 (85%) investigations, a failure of the facility consultant pharmacist to identify the inappropriate antipsychotic use upon their review and notify the facility in their monthly generated medication regimen review reports completed for each resident (in 2 of 29 investigations, the consultant pharmacist had not yet had the opportunity to review the resident's medication regimen).
- In 18 of 29 investigations, facilities receiving pharmacist consultant services below cost (62%).
- In 16 of 29 investigations, inadequate development of nursing care plans for antipsychotic use (55%).
- In 14 of 29 investigations, inadequate adherence to informed consent regulatory requirements (48%).

One investigative finding includes a resident on three antipsychotics continuously since her admission ten months prior to the complaint investigation. Clinical record review and interviews established there was no clinical justification to warrant the use of three antipsychotics concurrently—including potential risks, side effects and/or patient harm.

The facility's consultant pharmacist had failed to identify any concerns/issues related to the use of three antipsychotics.

Consultant Pharmacist Failure to Identify Inappropriate Antipsychotic Use

The consultant pharmacist is retained by the nursing home to ensure the overall quality of pharmaceutical services and, ultimately, safe and effective medication use. The consultant pharmacist provides his/her services via execution of a contract between the facility and the pharmacist (independent) or the pharmacist's employer (e.g., PharMerica, Omnicare, etc.). Pursuant to state and federal requirements, the consultant pharmacist must review each resident's medication regimen monthly, identify actual or potential irregularities (e.g., inappropriate antipsychotic use) and report these irregularities to the physician, administrator and director of nursing in a written report. Additionally, regulations require the facility to act upon the recommendations of the consultant pharmacist.

In the 29 investigations where inappropriate antipsychotic use was cited, and the facility consultant pharmacist had previously reviewed the resident's medication regimen (27 occurrences), he/she failed to identify and report the inappropriate use 23 times (85% of the time). The failure of the pharmacists to identify the inappropriate use of antipsychotic medication placed these residents at risk for potential side effects and/or harm.

During these investigations, as established in interviews with facility consultant pharmacists, two recurring factors were found to contribute to their failure to identify medication related issues: corporate workload mandates, and knowledge deficits/competency issues related to standards of practice around geriatric/adult pharmacotherapy, especially as related to antipsychotic drug use. Consultant pharmacists stated there is pressure to review 10 to 12 resident charts per hour (approximately five to six minutes per resident).

Receipt of Consultant Pharmacist Services at Below Cost

During the antipsychotic collaborative investigations, consultant pharmacist contracts are reviewed for services provided and fees associated with those services. State regulation stipulates a facility shall not accept money, goods or services free or below cost from any pharmacist or pharmacy as compensation or inducement for referral of business to any pharmacy (Title 22, Section 72353[d]). Of the facilities cited for use of inappropriate antipsychotic use, 62% (18 of 29) were also cited for receipt of consultant pharmacist services below cost.

In September 2008, the United States Department of Health and Human Services Office of Inspector General (HHS-OIG) released a report, "Supplemental Compliance Program Guidance for Nursing Facilities," in which concern over such contractual relationships was expressed as being "potentially disguised remuneration for referrals between the parties to the contract—in violation of the Federal Anti-Kickback Statute."^[15]

Nursing Care Plan Issues

Medications used for behavior control, such as antipsychotic medications, must be identified in a plan of care; the facility must specify behavioral data to be collected so that the effectiveness of the medications and occurrence of adverse effects can be monitored. State regulations further require that the behavioral data are collected and made available to the prescriber in a consolidated manner at least monthly. The intent of this requirement is to provide the prescriber with data to inform his/her clinical assessment of the effectiveness of the antipsychotic use and identification of adverse effects that would warrant reduction or discontinuation of the medication. Care planning is an interdisciplinary process and should be updated at least quarterly, or when there is a change in a resident's condition.

In 16 of the 29 investigations (55%), plans of care had not been developed or were incomplete. In 13 of these 16 investigations (81%), the facility had failed to identify the behavior to evaluate therapeutic effectiveness or pertinent medication side effects to be monitored. In 3 of 16 (19%), the antipsychotic plans of care were incomplete and/or inaccurate in that they did not identify the correct behaviors or side effects for monitoring.

Failure to develop an accurate and complete antipsychotic medication plan of care translates to a failure to provide the prescriber with accurate information to inform his/her clinical decision to continue or discontinue the use of the medication. Additionally, failure can result in the adverse effects of antipsychotic medication use going undetected and therefore not addressed or treated.

Informed Consent Issues

Informed consent is a patient right defined by state regulation as, "The voluntary agreement of a patient or a representative of an incapacitated patient to accept treatment...after receiving appropriate information" related to that treatment (e.g., use of antipsychotic medications). For antipsychotic medications, a physician or surgeon must obtain informed consent as required by health and safety code (Health and Safety Code 1418.9).

In 14 of the 29 investigations (48%), the facility was cited for non-compliance with applicable informed consent requirements. Of these non-compliances, the majority involved failure to offer evidence that informed consent was provided, or consent was obtained after the antipsychotic medication was initiated. Secondary reasons included the facility's failure to develop or implement an informed consent policy and procedure, and failure to include material information during the informed consent process, such as pertinent antipsychotic side effect information or risk/benefit of use based on FDA-mandated boxed warning information. In several investigations, it was apparent that a licensed nurse or ward clerk was providing material information related to antipsychotics, which is statutorily a physician's responsibility. In one investigation, a

family member denied she received information regarding her husband's antipsychotic therapy, stating she had not provided consent for its use.

Licensing & Certification continues to reiterate the importance, process and responsibility of antipsychotic informed consent in skilled nursing facilities, through these collaborative investigations, as well as through provider outreach and education-related activities—for example, issuance of two All Facility Letters (AFLs),^[16, 17] and webinars for the California Association of Health Facilities (CAHF).

Summary of Findings

The collaborative identified multiple quality of care issues related to antipsychotic use during 42 nursing home investigations over a 16-month period. These investigative findings demonstrate an opportunity for improvement in the use of these medications related to:

- Providing residents and their designated representatives with accurate and complete information to make informed decisions regarding the use of antipsychotic medications;
- Ensuring appropriate use of antipsychotic medications by considering non-pharmacologic interventions along with risk and benefits associated with the medication prior to using the antipsychotic;
- Developing and implementing a complete and accurate care plan related to behavioral modifications and antipsychotic use; and,
- Provision of quality consultant pharmacist services.

The collaborative, while successful in identifying quality of care issues, is limited by the scope of DHCS Medi-Cal claims data, in that only residents whose medications are reimbursed by Medi-Cal can be identified for focused review by L&C pharmaceutical consultant surveyors. The majority of nursing home residents receive their medications under the Medicare Part D program. It is unclear if medication reimbursement methodology (Medi-Cal versus Medicare) would otherwise influence the findings of the collaborative.

Recommendations for Improving the Use of Antipsychotics in Nursing Homes

The collaborative findings demonstrate a need for additional efforts to improve the appropriateness of antipsychotic use in nursing homes. The following recommendations fall under three broad areas: enforcement, education and establishment of a stakeholder workgroup.

Enforcement - Expansion of the Collaborative

The collaborative project continues, and will be expanded to further efforts to improve the care of nursing home residents and decrease the inappropriate use of antipsychotic medication.

During the first quarter of 2012, L&C incorporated the use of federal regulations found in 42 Code of Federal Regulations in the investigative process to be assessed by L&C PC surveyors. This will promote a robust application of both state and federal regulations pertaining to quality medication therapy in skilled nursing facilities ("dual enforcement" of both federal and state regulations as appropriate). It is anticipated more deficiencies will be generated, as there are federal regulations not mirrored in state regulations, such as the requirement for "gradual dose reduction" for antipsychotic medication use.

Effective August 1, 2012, the collaborative will further be expanded through development and implementation of a methodology for identifying facilities with a high rate of antipsychotic medication use (e.g., 50% or greater utilization for residents without a diagnosis of serious mental illness) by utilizing Minimum Data Set (MDS) 3.0 which would trigger an in-depth review. This methodology will be applied to all nursing homes scheduled for their annual federal recertification survey. The use of MDS data will address the limitation of Medi-Cal data, as the MDS is generated for all residents regardless of payer.

Surveyors will receive additional training, as well as a survey tool to evaluate the appropriate use of antipsychotic medications, including informed consent and provision of pharmaceutical consultant requirements. For these reasons the department anticipates implementation of the new survey process August 1, 2012.

Education

The medication use process in nursing homes involves a number of activities such as prescribing by physicians, administering and monitoring medications by nurses, and monthly medication regimen reviews by consultant pharmacists. The use of medications in nursing homes is complex, multidisciplinary in nature, and involves a number of state and federal regulations and laws that impact the use of medications. For these reasons, CDPH has shared the collaborative findings with multiple stakeholders (providers, professional organizations, etc.) and participated in a number of educational webinars and seminars with the intent that these groups would act upon our findings to modify current practices. The findings have been shared with the following organizations:

- Centers for Medicare & Medicaid Services Region IX and Central Office;
- California Association of Healthcare Facilities;
- California Association of Nursing Home Reform;
- Health Services Advisory Group;
- State Department of Justice, Bureau of Medi-Cal Fraud & Elder Abuse;
- State Board of Pharmacy;
- California Association of Long Term Care Medicine;
- DHCS Drug Utilization Review Board;
- DHCS Medi-Cal Pharmacy Benefits Division;
- California Pharmacists Association;
- American Society of Consultant Pharmacists (California Chapter); and,
- PharMerica.

In addition to continuing these efforts, CDPH will work with stakeholders and subject matter experts to prepare educational materials for facilities to ensure their understanding of the problem, as well as to provide potential solutions. The solution-based information may include guidelines, work aids, and sample policies and procedures directed at improving the informed consent process, care plan development and appropriate use of antipsychotic medication. The stakeholders will include but are not limited to:

- California Medical Board
- California Board of Pharmacy
- California Association of Healthcare Facilities
- California Pharmacists Association
- California Association of Long Term Care Medicine
- American Society of Consultant Pharmacists (California Chapter)

Referrals to Licensing Boards

Inappropriate use of antipsychotic medication is a multidisciplinary problem. CDPH is coordinating with professional licensing boards to develop guidelines for referral of health care practitioners to their respective boards when such a referral is warranted.

Next Steps to Decrease Inappropriate Antipsychotic Medication Use

CDPH, along with the DHCS, will convene a stakeholder workgroup composed of representatives from the health care industry, advocacy organizations, consumers and professional organizations that will be tasked with a number of activities to include:

- Providing recommendations on inclusion of national initiatives such as CMS' program aimed at improving behavioral health management and reducing use of antipsychotic medications in nursing homes;
- Evaluating the effectiveness of CDPH's enhanced enforcement actions and provide recommendations to further refine regulatory oversight activities;
- Evaluating options to strengthen the quality of consultant pharmacist services; and,
- Preparing and evaluating the content of educational materials aimed at reducing inappropriate use of antipsychotic medications.

Conclusion

The California Department of Public Health, in collaboration with its stakeholders, is committed to ensuring provision of quality medication therapy to Californians residing in nursing homes. Implementation of the aforementioned recommendations and next steps will assist in the reduction of unnecessary use of antipsychotic medications and reduce harmful side effects as well as reducing associated health care costs.

References

- [1] Briesachler BA, et al. The Quality of Antipsychotic Drug Prescribing in Nursing Homes. *Archives of Internal Medicine*. 2005; 163: 1280.
- [2] CMS Online Survey, Certification and Reporting (OSCAR) data 2010, 2011, and 2012 QIES link: <https://web.qiesnet.org/qiestosuccess/>
- [3] Beers M, Avorn J, Soumerai S, Everitt D, Sherman D, Salem S. Psychoactive medication use in intermediate-care facility residents. *JAMA* 1988;260:3016-20.
- [4] Ray WA, Federspiel CF, Schaffner W. A study of antipsychotic drug use in nursing homes: epidemiologic evidence suggesting misuse. *Am J Public Health* 1980;70:485-91.
- [5] FDA Public Health Advisory: Deaths with antipsychotics in elderly patients with behavioral disturbances 04/11/2005.
www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm053171.
- [6] FDA Information for Healthcare Professionals: Conventional Antipsychotics 6/16/2008.
www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124830.htm.
- [7] HHS-OIG report, May 2011, "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents": In May 2011, the Office of Inspector General of the Department of Health and Human Services issued a report, "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents."
<http://oig.hhs.gov/oei/reports/oei-07-08-00150.asp>
- [8] Inappropriate antipsychotic use, as defined above, is stipulated in 42 CFR 483.25 (l) for certified nursing homes as set forth and regulated by CMS.
http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/som107ap_pp_guidelines_ltcf.pdf
- [9] Lehman, A.F., Lieberman, J.A., Dixon, L.B., et al. (2004). Practice guideline for the treatment of patients with schizophrenia, second edition. *Am J Psychiatry*, 161, 1-56.
- [10] Kogut, S.J., Yam, F., & Dufresne, R. (2005). Prescribing of antipsychotic medication in a medicaid population: use of polytherapy and off-label dosages. *J Manag Care Pharm*, 11, 17-24.
- [11] Covell, N.H., Jackson, C.T., Evans, A.C., Essock, S.M. (2002). Antipsychotic prescribing practices in Connecticut's public mental health system: rates of changing medications and prescribing styles. *Schizophr Bull*, 28, 17-29.

[12] Ganguly, R., Kotzan, J.A., Miller, L.S., Kennedy, K., & Martin, B.C. (2004). Prevalence, trends, and factors associated with antipsychotic polypharmacy among Medicaid-eligible schizophrenia patients, 1998-2000. *Journal of Clinical Psychiatry*, 65, 1377-88.

[13] Stahl, S.M. & Grady, M.M. (2004). A critical review of atypical antipsychotic utilization: comparing monotherapy with polypharmacy and augmentation. *Curr Medication Chem*, 11, 313-27.

[14] Pollock, B., Forsyth, C., & Bies, R. (2009). The critical role of clinical pharmacology in geriatric psychopharmacology. *Clin Pharmacol Ther*, 85, 89-93.
Davies, A., Vardeva, K., Loze, J.Y., & L'Italien, G.J., Sennfalt K, van Baardewijk M. (2008). Cost-effectiveness of atypical antipsychotics for the management of schizophrenia in the UK*. *Curr Med Res Opin*, 24(11), 3275-3285.

[15] *OIG Supplemental Compliance Program Guidance for Nursing Facilities*, 73 Fed. Reg. 56832 (September 30, 2008).
http://oig.hhs.gov/fraud/docs/complianceguidance/nhg_fr.pdf

[16] AFL 11-08, January 7, 2011, Informed Consent.
<http://www.cdph.ca.gov/certlic/facilities/Documents/LNC-AFL-11-08.pdf>

[17] AFL 11-31, April 12, 2011, Questions and Answers About Informed Consent.
<http://www.cdph.ca.gov/certlic/facilities/Documents/LNC-AFL-11-31.pdf>

Appendix A

What are antipsychotic medications?

Antipsychotic medications belong to a broader category of medications known as psychopharmacologic medications. Psychopharmacological medication is any medication used for treating disruptive behavior, regulating and stabilizing mood, or treating psychiatric disorders. California statute, at Health and Safety Code (H&SC) 1418.9(c)(3), defines an "antipsychotic medication" as being "a medication approved by the United States Food and Drug Administration (FDA) for the treatment of psychosis." In California's skilled nursing facilities (SNFs), only a physician and surgeon may prescribe, order or increase an order for an antipsychotic medication.

An antipsychotic is a psychiatric medication primarily used to manage psychosis (including delusions or hallucinations, as well as disordered thought), particularly in schizophrenia and bipolar disorder, and is increasingly being used in the management of non-psychotic disorders. A first generation of antipsychotics, known as typical antipsychotics, was discovered in the 1950s. Most of the drugs in the second generation, known as atypical antipsychotics, have been developed more recently, although the first atypical antipsychotic, clozapine, was discovered in the 1950s and introduced clinically in the 1970s. Both generations of medication tend to block receptors in the brain's dopamine pathways, but antipsychotic drugs encompass a wide range of receptor targets. (<http://en.wikipedia.org/wiki/Antipsychotic>)

Antipsychotic Medications: Brand Name (Generic Name)

First generation or typical antipsychotic medications:

- chlorpromazine (generic only)
- fluphenazine (generic only)
- Haldol (haloperidol)
- Loxitane (loxapine)
- Moban (molindone)
- Navane (thiothixene)
- perphenazine (generic only)
- thioridazine (generic only)
- trifluoperazine (generic only)

Second generation or atypical antipsychotic medications:

- Abilify (aripiprazole)
- Clozaril (clozapine)
- Fanapt (iloperidone)
- Geodon (ziprasidone)
- Invega (paliperidone)
- Risperdal (risperidone)
- Seroquel (quetiapine)
- Zyprexa (olanzapine)

Combination antidepressant and antipsychotic medication:

- Symbyax (Prozac & Zyprexa) fluoxetine & olanzapine